IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

Ravgen, Inc., Plaintiff, v. Progenity, Inc., Defendant.	Civil Action No. _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Ravgen, Inc. ("Ravgen"), for its Complaint against Defendant Progenity, Inc. ("Progenity"), hereby alleges as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 7,727,720 (the "'720 Patent") and 7,332,277 (the "'277 Patent") (collectively the "Patents-in-Suit"), arising under the Patent Laws of the United States, 35 U.S.C. §§ 271 *et seq*.

THE PARTIES

2. Plaintiff Ravgen is a Delaware corporation with its principal place of business at 9241 Rumsey Rd., Columbia, MD 21045. Ravgen is a pioneering diagnostics company that focuses on non-invasive prenatal testing. Ravgen has spent millions of dollars researching and developing novel methods for the detection of cell-free DNA to replace conventional, invasive procedures. Ravgen's innovative cell-free DNA technology has various applications, including non-invasive prenatal and other genetic testing. Those efforts have resulted in the issuance of several patents, including the Patents-in-Suit.

3. Defendant Progenity is a company organized and existing under the laws of the State of Delaware, with its principal place of business at 4330 La Jolla Village Drive, Suite 200, San Diego, California, 92122. (Ex. 5 (Progenity Inc. Form 10-Q, September 30, 2020) at 1.) Progenity has appointed Cogency Global, Inc., 850 New Burton Road, Suite 201, Dover, Delaware 19904 as its agent for service of process. (Ex. 6 (Eighth Amended & Restated Certificate of Incorporation) at 1 (https://investors.progenity.com/static-files/841f34f1-ae3a-4cec-a9cd-c0d58180e53e); Ex. 7 (State of Delaware Entity Status for Progenity, Inc.).)

4. Progenity, itself and/or through its subsidiaries and affiliates, makes, uses, and commercializes noninvasive prenatal tests that utilize massively parallel sequencing (MPS) across the whole genome to analyze circulating cell-free DNA (cfDNA) extracted from a maternal blood sample to test for common chromosome aneuploidies, marketed under the tradename "Innatal."

5. Progenity, itself and/or through its subsidiaries and affiliates, makes, uses, and commercializes noninvasive prenatal tests that apply cfDNA testing to detect common chromosomal diseases and rare monogenic diseases caused by variants in a specific gene, marketed under the tradename "Resura."

6. Progenity offers and markets tests under the Innatal and Resura tradenames throughout the United States, including without limitation through the website www.progenity.com. (*See generally* Ex. 8 (https://www.progenity.com/products/innatal); Ex. 9 (https://www.progenity.com/products/resura).)

JURISDICTION AND VENUE

7. Ravgen incorporates by reference paragraphs 1–6.

8. This action arises under the patent laws of the United States, including 35 U.S.C. §§ 271 *et seq*. The jurisdiction of this Court over the subject matter of this action is proper under 28 U.S.C. §§ 1331 and 1338(a).

9. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391(b), (c), and 1400(b). Progenity is an entity organized under the laws of Delaware and reside in Delaware for purposes of venue under 28 U.S.C. § 1400(b). Progenity conducts business in Delaware, at least by offering for sale and selling products and services through its website, which is accessible in Delaware. Progenity has also committed and continues to commit acts of infringement in this District.

10. This Court has personal jurisdiction over Progenity because Progenity conducts business in Delaware by at least offering for sale or selling products and services through its website, which is accessible in Delaware, and because infringement has occurred and continues to occur in Delaware.

11. Personal jurisdiction also exists over Progenity because it is an entity organized under the laws of Delaware.

BACKGROUND OF THE INVENTION

12. Dr. Ravinder S. Dhallan is the founder of Ravgen, Inc. and the inventor of several patents in the field of detection of genetic disorders, including chromosomal abnormalities and mutations. Ravgen's mission is to provide state of the art genetic testing that will enrich the lives of its patients. For example, through the use of its novel techniques in non-invasive prenatal diagnostic testing, Ravgen gives patients the knowledge they need to prepare for their pregnancies and treat diseases at an early stage.

13. Prior to founding Ravgen, Dr. Dhallan was a board-certified emergency room physician. Between starting medical school at Johns Hopkins University and shortly after his

residency at Mass General (Harvard University School of Medicine), Dr. Dhallan and his wife suffered three miscarriages. At that time, the prenatal diagnostic testing procedures available included (a) non-invasive techniques with low sensitivity and specificity, and (b) tests with higher sensitivity and specificity that were highly invasive and therefore associated with a risk for loss of pregnancy. After discovering the limitations on the available techniques for prenatal testing, Dr. Dhallan made it his mission to invent an improved prenatal diagnostic exam—one that was both non-invasive and accurate. In September of 2000, Dr. Dhallan founded Ravgen (which stands for "Rapid Analysis of Variations in the GENome") to pursue that goal.

14. Prior to Ravgen's inventions, scientists had recognized the need for a genetic testing technique that used "cell-free" or "free" fetal DNA circulating in maternal blood. A technique that relied on circulating free fetal DNA would require only a simple blood draw from the mother and would therefore be an improvement over invasive diagnostic tests.

15. However, at that time, the use of free fetal DNA for detecting chromosomal abnormalities was limited by the low percentage of free fetal DNA that could be recovered from a sample of maternal blood using existing techniques. (*See, e.g.*, Ex. 10 (Y.M. Dennis Lo et al., *Presence of Fetal DNA in Maternal Plasma and Serum*, 350 THE LANCET 768-75 (1997), https://doi.org/10.1016/S0140-6736(97)02174-0).) Dr. Dhallan recognized that a method that could increase the percentage of free fetal DNA relative to the free maternal DNA in a sample was necessary to the development of an accurate, non-invasive prenatal diagnostic test.

16. After substantial research, Dr. Dhallan conceived that including an agent that impedes cell lysis (disruption of the cell membrane) if cells are present during sample collection, shipping, handling, and processing would permit the recovery of a larger percentage of cell-free fetal DNA (relative to the cell-free maternal DNA in a sample). Dr. Dhallan hypothesized that

this new approach would decrease the amount of maternal cell lysis and therefore lower the amount of cell-free maternal DNA in the sample, thereby increasing the percentage of cell-free fetal DNA. He developed a novel method for processing cell-free fetal DNA that involved the addition of an agent that impedes cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—to maternal blood samples coupled with careful processing protocols. With that novel method, Dr. Dhallan was able to increase the relative percentage of cell-free fetal DNA in the processed sample.

17. Having successfully increased the relative percentage of cell-free fetal DNA recovered, Dr. Dhallan next addressed the challenge of distinguishing between the cell-free maternal and cell-free fetal DNA in a sample in order to determine whether a chromosomal abnormality is present in the fetal DNA. Prior to Ravgen's inventions, known methods for detecting fetal chromosomal abnormalities were time-consuming and burdensome. Many required amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product in a sample. Dr. Dhallan developed an alternate method that greatly increased the efficiency of this process by taking advantage of the variation of base sequences among different individuals (including a mother and fetus) ("alleles") at particular positions ("loci") on chromosomes. The term "allele" refers to an alternate form of a gene, or a non-coding region of DNA that occurs at a particular locus on a chromosome. The alleles present at certain loci on chromosomes (including, for example, "single nucleotide polymorphisms" or "SNPs") vary between different individuals. At such a locus, a fetus may therefore inherit an allele from its father that differs from the alleles present at that locus on its mother's chromosome. Dr. Dhallan developed a novel method for quantifying the allelic ratio at such a locus (or loci) of interest in a sample comprising maternal and fetal cell-free DNA in order to detect whether a fetal

chromosomal abnormality was present in the fetal DNA of the sample, without requiring physical separation of the fetal from the maternal cell-free DNA.

18. Dr. Dhallan understood that his breakthroughs laid the foundation for the development of accurate non-invasive prenatal diagnostic tests. For example, he published a paper in the *Journal of the American Medical Association* (*JAMA*) in 2004, explaining that "the methods described herein for increasing the percentage of cell-free fetal DNA provide a solid foundation for the development of a noninvasive prenatal diagnostic test." (Ex. 11 at 1119 (R. Dhallan et al., *Methods to Increase the Percentage of Free Fetal DNA Recovered from the Maternal Circulation*, 291 JAMA 1114–19 (2004), https://doi.org/10.1001/jama.291.9.1114).)

19. *JAMA* also ran an editorial alongside Dr. Dhallan's article in 2004, recognizing the significance of his inventions to applications in prenatal genetic diagnosis and cancer detection and surveillance:

> In this issue of THE JOURNAL, the findings reported in the study by Dhallan and colleagues on enhancing recovery of cell-free DNA in maternal blood have major clinical implications. Developing a reliable, transportable technology for cell-free DNA analysis impacts 2 crucial areas—prenatal genetic diagnosis and cancer detection and surveillance. In prenatal genetic diagnosis, detecting a fetal abnormality without an invasive procedure (or with fewer invasive procedures) is a major advantage. Likewise in cancer surveillance (eg, in patients with leukemia), monitoring treatment without having to perform a bone marrow aspiration for karyotype also would be of great benefit.
>
> * * *
>
> With prospective studies focusing on clinical applications of these findings, profound clinical implications could emerge for prenatal diagnosis and cancer surveillance.

(Ex. 12 at 1135, 1137 (J.L. Simpson & F. Bischoff, *Cell-Free Fetal DNA in Maternal Blood: Evolving Clinical Applications*, 291 JAMA 1135–37 (2004), https://doi.org/10.1001/jama.291.9.1135).)

20. In 2007, Dr. Dhallan published a second journal article in *The Lancet* that presented a study showcasing Ravgen's ability to use its novel technology to detect Down's syndrome using free fetal DNA in a maternal blood sample. (Ex. 13 (R. Dhallan et al., *A Non-Invasive Test for Prenatal Diagnosis Based on Fetal DNA Present in Maternal Blood: A Preliminary Study*, 369 THE LANCET 474–81 (2007), https://doi.org/10.1016/S0140-6736(07)60115-9).) Dr. Dhallan's peers at *The Lancet* also recognized that his innovative test "opens a new era in prenatal screening." (*See* Ex. 14 (A. Benachi & J.M. Costa, *Non-Invasive Prenatal Diagnosis of Fetal Aneuploidies*, 369 THE LANCET 440–42 (2007), https://doi.org/10.1016/S0140-6736(07)60116-0).)

21. Dr. Dhallan's publications received worldwide press coverage, from outlets such as CNN, BBC, and Washington Post. (*See* Ex. 15 (L. Palmer, *A Better Prenatal Test?*, CNN MONEY (Sept. 12, 2007), https://money.cnn.com/2007/09/07/smbusiness/amniocentesis.fsb/index.htm); Ex. 16 (*Hope for Safe Prenatal Gene Test*, BBC NEWS, Feb 2, 2007, http://news.bbc.co.uk/2/hi/health/6320273.stm); Ex. 17 (A. Gardner, *Experimental Prenatal Test Helps Spot Birth Defects*, WASH. POST (Feb. 2, 2007), https://www.washingtonpost.com/wp-dyn/content/article/2007/02/02/AR2007020200914.html).)

22. The Patents-in-Suit resulted from Dr. Dhallan's years-long research at Ravgen to develop these innovative new methods for detecting genetic disorders.

PATENTS-IN-SUIT

23. Ravgen incorporates by reference paragraphs 1–22.

24. The '277 Patent, entitled "Methods For Detection Of Genetic Disorders," was duly and legally issued by the United States Patent and Trademark Office on February 19, 2008. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the '277 Patent is attached hereto as Exhibit 1.

25. Ravgen is the exclusive owner of all rights, title, and interest in the '277 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the '277 Patent. (*See* Ex. 3.)

26. The '720 Patent, entitled "Methods For Detection Of Genetic Disorders," was duly and legally issued by the United States Patent and Trademark Office on June 1, 2010. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the '720 Patent is attached hereto as Exhibit 2.

27. Ravgen is the exclusive owner of all rights, title, and interest in the '720 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the '720 Patent. (*See* Ex. 4.)

28. The '277 Patent is directed to, among other things, novel methods used in the detection of genetic disorders. For example, claim 81 of the '277 Patent recites:

> A method for preparing a sample for analysis comprising isolating free fetal nucleic acid from a the sample, wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor.

29. The '720 Patent is directed to novel methods for detecting a free nucleic acid in a sample. For example, claim 1 of the '720 Patent recites:

> A method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; and (b) detecting the presence or absence of the free nucleic acid.

30. The Patents-in-Suit are directed to unconventional, non-routine techniques for preparing and analyzing extracellular circulatory DNA, including for the detection of genetic

disorders. The Patents-in-Suit explain that, *inter alia*, the inventions claimed therein overcame problems in the field—for example, that the low percentage of fetal DNA in maternal plasma makes using the DNA for genotyping the fetus difficult—with a novel and innovative solution—the addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample, which increase the percentage of cell-free DNA available for detection and analysis:

> The percentage of fetal DNA in maternal plasma is between 0.39-11.9% (Pertl, and Bianchi, *Obstetrics and Gynecology* 98: 483-490 (2001)). **The majority of the DNA in the plasma sample is maternal, which makes using the DNA for genotyping the fetus difficult**. However, methods that increase the percentage of fetal DNA in the maternal plasma allow the sequence of the fetal DNA to be determined, and allow for the detection of genetic disorders including mutations, insertions, deletions, and chromosomal abnormalities. **The addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample can increase the relative percentage of fetal DNA.** While lysis of both maternal and fetal cells is inhibited, the vast majority of cells are maternal, and thus by reducing the lysis of maternal cells, there is a relative increase in the percentage of free fetal DNA.

(Ex. 1 ('277 Patent) at 32:24–39; Ex. 2 ('720 Patent) at 33:31–46 (emphases added).)

31. The Patents-in-Suit teach that the benefit of Dr. Dhallan's discovery, an increase in the relative percentage of cell-free DNA, is realized by performance of the claimed method, including through the inclusion of an agent that inhibits the lysis of the cells in a sample:

> An overall increase in fetal DNA was achieved by reducing the maternal cell lysis, and thus, reducing the amount of maternal DNA present in the sample. In this example, formaldehyde was used to prevent lysis of the cells, however any agent that prevents the lysis of cells or increases the structural integrity of the cells can be used. Two or more than two cell lysis inhibitors can be used. The increase in fetal DNA in the maternal plasma allows the sequence of the fetal DNA to be determined, and provides for the rapid detection of abnormal DNA sequences or chromosomal abnormalities including but not limited to point mutation, reading frame shift, transition, transversion, addition, insertion, deletion, addition-deletion, frame-shift, missense, reverse mutation, and microsatellite alteration, trisomy, monosomy, other aneuploidies, amplification,

> rearrangement, translocation, transversion, deletion, addition, amplification, fragment, translocation, and rearrangement.

(Ex. 1 ('277 Patent) at 91:44–60; Ex. 2 ('720 Patent) at 92:10–26.)

32. For example, during the prosecution of the '720 Patent at the Patent and Trademark Office, Ravgen explained that the innovative concept of using agents that inhibit cell lysis during cell-free DNA detection and analysis is recited by the claimed methods of the '720 Patent, including in claim 1:

> Applicant has discovered that the addition of a cell lysis inhibitor to a sample prior to detecting the presence of free nucleic acid can ***significantly and unexpectedly*** increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample.
>
> * * *
>
> The methods disclosed in claims 1-8, 21-23, and 26 serve a long-felt need in the medical community, and provide unexpected results, and are therefore non-obvious.

(Ex. 18 ('720 File History, June 2, 2009 Response to Office Action) at 12, 14 (emphasis added).)

33. The inventive concept of the Patents-in-Suit of including an agent that inhibits cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—with a sample represented a significant improvement in the preparation of samples used for non-invasive testing, including non-invasive prenatal testing to unmask previously undetectable fetal genetic traits. At the time of the invention, it would not have been routine or conventional to add an agent that inhibits cell lysis to a sample to increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample. In fact, as described above, that inventive concept was recognized by Dr. Dhallan's peers as "an important step in improving detection of cell-free DNA." (Ex. 12 at 1137.)

34. The '277 Patent is further directed to an unconventional, non-routine method of detecting fetal chromosomal abnormalities which involves "quantitating a ratio of the relative

amount of alleles in a mixture of maternal DNA and fetal DNA." (Ex. 19 ('277 File History, May 30, 2007 Response to Office Action) at 30.) For example, claim 1 of the '277 Patent recites:

> A method for detecting the presence or absence of a fetal chromosomal abnormality, said method comprising: quantitating a ratio of the relative amounts of alleles at a heterozygous locus of interest in a mixture of template DNA, wherein said mixture comprises maternal DNA and fetal DNA, and wherein said mixture of maternal DNA and fetal DNA has been obtained from a sample from a pregnant female, and further wherein said heterozygous locus of interest has been identified by determining the sequence of alleles at the locus of interest, and wherein said ratio indicates the presence or absence of a fetal chromosomal abnormality.

35. The '277 Patent explains that this claimed method represented a significant improvement over prior art methods of detecting fetal chromosomal abnormalities, many of which were costly, time-consuming, and burdensome because they either required the amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product. (Ex. 1 at 66:14-20.) By contrast, the claimed "ratio" method of the '277 Patent only requires sequencing of discrete "loci of interest" (such as "single nucleotide polymorphisms," or "SNPs") from the collected DNA sample. (*Id.* at 34:63-35:37 ("In fact, it is an advantage of the invention that primers that copy an entire gene sequence need not be utilized. . . . There is no advantage to sequencing the entire gene as this can increase cost and delay results. Sequencing only the desired bases or loci of interest maximizes the overall efficiency of the method because it allows for the sequence of the maximum number of loci of interest to be determined in the fastest amount of time and with minimal cost."); *Id.* at 35:28-37.)

36. During the prosecution of the '277 Patent at the Patent and Trademark Office, Ravgen gave the following example of an implementation of the claimed "ratio" method:

> Applicants have invented a method for detecting the presence or absence of a fetal chromosomal abnormality, wherein the method

> comprises, inter alia, quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA.
>
> ***
>
> [R]atios were calculated at both chromosomes 13 and 21 in a heterogeneous mixture of 75% Down syndrome DNA and 25% maternal DNA. Single nucleotide polymorphisms were analyzed wherein the maternal genome was homozygous for one allele at a specific genetic site and the Down syndrome DNA was heterozygous at the same genetic site. If at a certain site, the maternal genome contains an adenine at both copies of chromosome 13, and the Down syndrome genome is comprised of one chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.60 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.25 + 0.25 maternal A alleles).
>
> On the other hand, if at a certain genetic site on chromosome 21, the maternal genome contains an adenine at both copies of chromosome 21, and the Down syndrome genome is comprised of two chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.375 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.75 Down syndrome A allele + 0.25 + 0.25 (maternal A alleles). Thus, the methods described in the present application detect chromosomal abnormalities using a method that comprises, inter alia, quantitating a ratio of alleles in a heterogeneous mixture of DNA, wherein the ratio represents alleles from more than one individual.

(Ex. 19 ('277 File History, May 30, 2007 Response to Office Action) at 30.)

DEFENDANT'S INFRINGING ACTIVITIES

37. Ravgen incorporates by reference paragraphs 1–36.

A. The Accused Innatal Prenatal Screen

38. In 2015, Progenity launched the Innatal® Prenatal Screen, a noninvasive prenatal screening test to screen for chromosome abnormalities through the analysis of cfDNA at or after 10 weeks of gestation. (*See* Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 120.) In 2019, Progenity upgraded the Innatal Prenatal Screen with the latest sequencing technology, improved chemistry, and bioinformatics analysis. (Ex. 21 (https://investors.progenity.com/news-

releases/news-release-details/progenity-launches-first-commercially-available-custom-designed#:~:text=%C2%AB%20Back-,Progenity%20launches%20first%20commercially%20available%2C%20custom%2Ddesigned%2C%20noninvasive,prenatal%20test%20for%20monogenic%20diseases&text=Progenity%20also%20announces%20improvements%20to,across%20all%20common%20chromosomal%20aneuploidies).) Progenity is currently developing the next generation Innatal Prenatal Screen (Innatal 4th Generation) and anticipates a commercial launch by the end of 2021. (Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 124.)

39. The Innatal® Prenatal Screen analyzes cfDNA extracted "from a maternal blood sample to assess the pregnancy for common chromosome aneuploidies." (Ex. 22 (https://www.progenity.com/products/innatal#practice).)

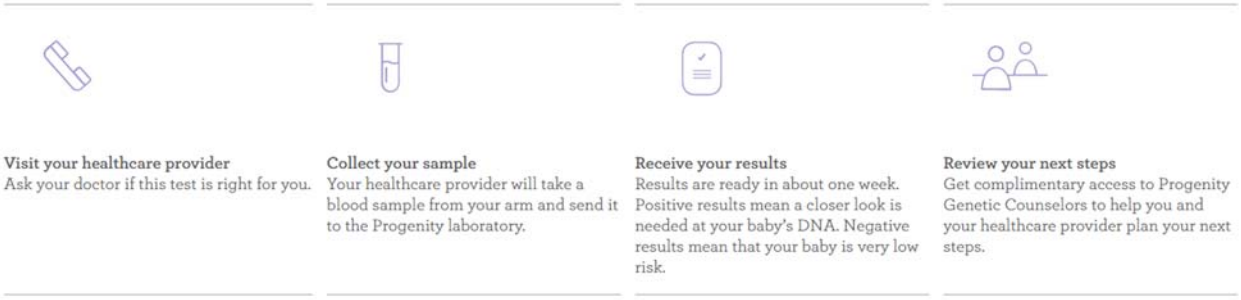
40. The Innatal Prenatal Screen requires samples containing an agent that inhibits cell lysis. For example, Progenity lists "10 ml Streck DNA tube" as the required collection container for the Innatal® test. (*See*, *e.g.*, Ex. 23 at 1 (https://www.progenity.com/sites/default/files/PG_OCRRequisition_WH-23035-01_eform082520.pdf); Ex. 24 (https://www.progenity.com/sites/default/files/PG_WomensHealthSpecimenGuide_WH-16001-01_092020_FINAL.pdf) (indicating that only blood collected in a 10 mL black-and-tan-top Streck tube will be accepted for the Innatal® test); Ex. 25 (https://www.streck.com/products/stabilization/cell-free-dna-bct/) (showing that the black and tan top Streck tubes are Streck Blood Collection Tubes (BCT™) tubes).) Providers of the Innatal Prenatal Screen also list "1 x 10mL provided cell-free DNA streck BCT tube" as a required material for specimen collection. (*See*, *e.g.*, Ex. 26 at 61 (https://www.ap2.com/wp-

content/uploads/2017/04/2017-directory-services-digital.pdf); *See also*, Ex. 27 (https://www.wadsworth.org/progenity-inc-6) ("**Specimen type:** whole blood: maternal in Streck Cell-Free DNA BCT").)

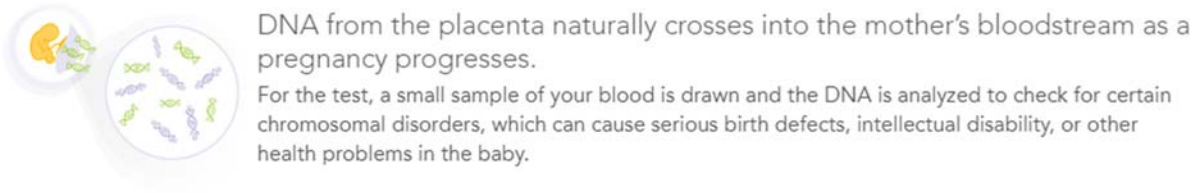
41. Progenity-funded scientific articles analyzing the Innatal Prenatal Screen confirm the use of Streck Blood Collection Tubes (BCT™) tubes to collect samples for the Innatal Prenatal Screen. (*See*, *e.g.*, Ex 28 (https://www.progenity.com/clinical-publications/proven-performance-prenatal-screen#innatal) (referencing Porreco et al., *Evaluation of a novel screening method for fetal aneuploidy using cell-free DNA in maternal plasma*, J. MED. SCREENING (2019) as providing data supporting performance of the Innatal Prenatal Screen); Ex 29 at 4 (Porreco et al., *Evaluation of a novel screening method for fetal aneuploidy using cell-free DNA in maternal plasma*, J. MED. SCREENING (2019), https://doi.org/10.1177%2F0969141319873682) ("Venous blood (approximately 20 mL) was collected from study participants in a ***cell-free BCT tube (Streck. Omaha, NE, USA)***. Sample tubes were shipped directly to Progenity, Inc. for processing and storage within five days of collection.") (funded by Progenity).)

42. The Streck Cell-Free DNA Blood Collection Tube ("BCT") includes an agent that inhibits cell lysis. A Streck Cell-Free DNA BCT "stabilizes nucleated blood cells. The unique preservative ***limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA***. Cell-Free DNA BCT has also been demonstrated to minimize the degradation of circulating tumor cells (CTCs). By ***limiting cell lysis***, the specialized chemistry provides sample integrity during storage, shipping and handling of blood samples. Cell-free DNA and gDNA are stable for up to 14 days at 6 °C to 37 °C. CTCs are stable for up to 7 days at 15 °C to 30 °C." (Ex. 25 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/)).)

43. In processing the Innatal Prenatal Screen, Progenity isolates cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT and then analyzes the isolated fetal cell-free DNA to detect chromosomal abnormalities as shown below:



(Ex. 8 (https://www.progenity.com/products/innatal#basics);



id.; *see also id.* (displaying video entitled "*Prepare for Life*") at 1:22-44 ("Cell-free DNA is actually what we are looking at. Cell-free DNA from the placenta of the pregnancy. Naturally during pregnancy, DNA fragments from the placenta cross into mom's bloodstream and starting at 10 weeks gestation ***we can actually identify this DNA and look at it to see would a baby be at an increased risk for a chromosomal disorder***."); Ex. 22 (https://www.progenity.com/products/innatal#practice) ("Cell-free DNA (cfDNA) is analyzed from a maternal blood sample to assess the pregnancy for common chromosome aneuploidies . . . . The Innatal Prenatal Screen utilizes massively parallel sequencing (MPS) across the whole genome. . . . The reads are counted to determine whether the sample has extra or missing reads from a particular chromosome. . . . Fetal fraction is determined for each sample using a proprietary algorithm."); Ex. 29 at 2 ("This study aimed to detect all fetal whole chromosome abnormalities

on chromosomes 13, 16, 18, 21, X, and Y, through analysis of cfDNA in maternal blood, utilizing a novel sequence targeting approach using molecular inversion probes (MIPs)").)

44. On information and belief, Progenity licenses the right to perform the Innatal Prenatal Screen to third party laboratories. For example, "a portion of [Progenity's] tests are performed by third-party CLIA certified laboratories." (Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 33.) Progenity enters into contracts with these third-party laboratories and the third-party laboratories are subject to contractual obligations. (*Id.* ("These third-party laboratories are subject to contractual obligations[.]").)

B. The Accused Resura Prenatal Test

45. On April 2, 2019, Progenity announced the launch of the Resura® Prenatal Test for Monogenic Disease, a customizable, non-invasive prenatal test for single gene disorders. (*See* Ex. 21 (https://investors.progenity.com/news-releases/news-release-details/progenity-launches-first-commercially-available-custom-designed#:~:text=%C2%AB%20Back-,Progenity%20launches%20first%20commercially%20available%2C%20custom%2Ddesigned%2C%20noninvasive,prenatal%20test%20for%20monogenic%20diseases&text=Progenity%20also%20announces%20improvements%20to,across%20all%20common%20chromosomal%20aneuploidies).)

46. The Resura® Prenatal Test "uses fetal cell-free DNA (cfDNA) extracted from a sample of the mother's blood to test for genetic variants." (*Id.*; *see also* Ex. 30 (https://www.progenity.com/products/resura#practice) ("The Resura Prenatal Test is a new application of cfDNA technology that allows you to detect not only common chromosomal diseases, but also rare monogenic diseases caused by variants in a specific gene.").)

47. The Resura Prenatal Test requires samples containing an agent that inhibits cell lysis. For example, Progenity states that "a blood sample—***six 10mL Streck DNA Tubes***—from the pregnant mother (10+ weeks' gestation) ***is required*** for [Resura] prenatal testing." (Ex. 30 (https://www.progenity.com/products/resura#practice) (emphases added); *see also*, Ex. 23 (https://www.progenity.com/sites/default/files/PG_OCRRequisition_WH-23035-01_eform082520.pdf); Ex. 31 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) (poster presenting research results for the Resura Prenatal Test) ("**Samples:** Blood is collected from pregnant patients at ≥ 10 weeks gestational age in a Streck BCT® and transported overnight to the Progenity lab.").)

48. As described above, samples collected in Streck Cell-Free DNA BCT tubes, including blood samples, contain an agent that inhibits cell lysis. (*See, e.g.*, Ex. 25 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/) (product documentation for the Streck Cell-Free DNA BCT® blood collection tube).)

49. In processing the Resura Prenatal Test, Progenity isolates and sequences cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT, and then analyzes the isolated fetal cell-free DNA to detect chromosomal abnormalities as shown below:

Step 3: Prenatal Testing

A blood sample—six 10mL Streck DNA tubes—from the pregnant mother (10+ weeks' gestation) is required for prenatal testing. The test looks for common chromosomal diseases along with the specific monogenic disease for which testing is requested. This step takes 1 – 2 weeks.

(Ex. 30 (https://www.progenity.com/products/resura#practice); Ex. 32 at 1 (https://www.progenity.com/sites/default/files/PG_Resura_ClinicalDataSummarySheet_WH-02028-01_022020_FINAL.pdf) ("The Resura® Prenatal Test uses a droplet digital PCR system to

amplify the region of interest within a gene. Amplification data is compared to expected results based on the mother's genotype and fetal fraction to predict whether the fetus is affected or unaffected. . . . The maternal genotype (allele ratio) that serves as a baseline will vary depending on the inheritance pattern. The baseline is 0.50 when the mother is heterozygous and 0.00 when she is homozygous for the allele of interest. The ratio detected in cfDNA will shift from this baseline according to the fetal status (i.e. affected or unaffected) and is relative to the fetal fraction."); Ex. 31 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) (poster presenting research results for the Resura Prenatal Test) ("**Samples**: . . . The tubes are centrifuged to separate the plasma. Cell-free DNA is extracted from maternal plasma using an internally developed bead-based method. **Fetal fraction determination**: A portion of the cfDNA is tested in triplicate using a NGS method for determination of the total fetal DNA contribution. **Fetal genotyping**: The BIORAD QX200TM Droplet Digital PCR system is used to perform a variant-specific probe-based assay. Measurements of the relative abundance of reference and alternate alleles are produced, resulting in the cfDNA allele ratio. **Data analysis**: The total fetal DNA contribution, the cfDNA allele ratio, and other run-based data are used to calculate the fetal status (affected vs unaffected) and the associated probability.").)

50. On information and belief, Progenity licenses the right to perform the Resura Prenatal Test to third party laboratories. For example, "a portion of [Progenity's] tests are performed by third-party CLIA certified laboratories." (Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 33.) Progenity enters into contracts with these third-party laboratories

and the third-party laboratories are subject to contractual obligations. (*Id.* ("These third-party laboratories are subject to contractual obligations[.]").)

C. Defendant's Knowledge Of The Ravgen Patents

51. The Patents-in-Suit claim advancements in the genetic testing industry in which Progenity actively participates and are widely acclaimed as breakthroughs in genetic testing. On information and belief, Progenity has been aware of the Patents-in-Suit and the fact that performance of the Progenity's cell-free DNA tests, including the Innatal and Resura Tests, practice the claimed inventions of those patents since at least the launch date of each of the infringing products.

52. Progenity has been and is the assignee of a number of patents and patent applications that are related to subject matter similar to the Patents-in-Suit and that were filed after the Patents-in-Suit were published. On information and belief, in researching the patentability of its own patents, Progenity did, or at a minimum should have, become aware of the Patents-in-Suit.

53. Progenity was also aware of the Patents-in-Suit through *inter partes* review proceedings at the Patent Trial and Appeal Board (PTAB).

54. Progenity initiated and is a party in Case Nos. IPR2021-00280 and IPR2021-00281 at the PTAB.

55. The petition in each of Case Nos. IPR2021-00280 and IPR2021-00280 included grounds asserting the application that lead to Ravgen's '277 Patent (U.S. Patent Application Publication No. 2004/0137470) as prior art against certain challenged claims. (*See generally* Ex. 37 (*Progenity, Inc. v. Natera, Inc.*, IPR2021-00280, Paper No. 2); Ex. 38 (*Progenity, Inc. v. Natera, Inc.*, IPR2021-00281, Paper No. 2).) The petitions were filed by Progenity on December 18, 2020. (Ex. 37 at 69; Ex. 38 at 69.)

56. Progenity has advanced substantive arguments regarding the application that lead to Ravgen's '277 Patent (U.S. Patent Application Publication No. 2004/0137470) in Case Nos. IPR 2021-00280 and IPR2021-00281 at the PTAB.

57. Progenity was also aware of the Patents-in-Suit through communications with Dr. Dhallan and Ravgen regarding Ravgen's technology and patent portfolio.

58. On September 23, 2015, Progenity, through Harry Stylli, contacted Dr. Dhallan. (Ex. 33 (Stylli Emails dated September 23, 2015 through October 5, 2015).) Mr. Stylli stated his contact was "long over due." (*Id.* at 2.) Mr. Stylli and Dr. Dhallan scheduled a call for October 8, 2015, to discuss Ravgen and its technology. (*Id.* at 1.)

59. After the phone call, Mr. Stylli emailed Dr. Dhallan on October 8, 2015, to schedule an in-person meeting at Ravgen to continue discussing Ravgen and its technology. (Ex. 34 (Stylli Emails dated October 8, 2015 through January 28, 2016).) Mr. Stylli met with Dr. Dhallan in person at Ravgen on or around October 15, 2015, to discuss Ravgen and its technology. (*Id.* at 3.)

60. Following the in-person meeting, Mr. Stylli emailed Dr. Dhallan on December 29, 2015. (*Id.* at 2-3.) Mr. Stylli stated that Progenity "concluded that we cannot meet the valuation objectives that [Dr. Dhallan] articulated during our meeting." (*Id.* at 3.) Mr. Stylli also stated that he "greatly respect[ed] [Dr. Dhallan's] many contributions to the prenatal field and admire[d] [Dr. Dhallan's] vision." (*Id.*)

61. Mr. Stylli and Dr. Dhallan discussed continuing their dialogue and spoke on or around January 20, 2016, regarding a second in-person meeting. (*Id.* at 1-2.) Mr. Stylli and Dr. Dhallan met in person at Progenity on or around February 18, 2016, and continued their discussions of Ravgen and its technology. (Ex. 35 (Stylli Emails dated January 30, 2016 through February 1, 2016).)

62. Despite its knowledge of the Patents-in-Suit and of its infringement of those patents, Progenity has continued to willfully infringe the Patents-in-Suit so as to obtain the significant benefits of Ravgen's innovations without paying compensation to Ravgen. For example, Progenity has continued to use the claimed methods in their Innatal and Resura Tests without a license, and, on information and belief, has generated hundreds of millions of dollars in revenue from its infringement. Additionally, after becoming aware of the Patents-in-Suit, Progenity proceeded to commercialize the Innatal and Resura Tests built on and including the claimed inventions of the Patents-in-Suit without entering into a license to the Patents-in-Suit.

COUNT I

(Infringement Of The '277 Patent)

63. Ravgen incorporates by reference paragraphs 1–62.

64. The '277 Patent is valid and enforceable.

65. Defendant Progenity has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including Progenity's Innatal Prenatal Screen and Resura Prenatal Test.

66. As one example, Progenity infringes at least Claim 81 of the '277 Patent by using the Innatal Prenatal Screen. For example, use of the Innatal Prenatal Screen requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 22 (https://www.progenity.com/products/innatal#practice) ("Cell-free DNA (cfDNA)

is analyzed from a maternal blood sample to assess the pregnancy for common chromosome aneuploidies, including trisomy 21 (Down syndrome), trisomy 18, trisomy 13, and sex chromosome abnormalities."); *see also* Ex. 29 at 3 ("Sample tubes were shipped directly to Progenity, Inc. for processing and storage . . . . The plasma supernatants from 96 samples (including controls) were transferred to deep well plates (Arctic White; Bethlehem, PA, USA) for cfDNA isolation . . . . Isolated cfDNA samples were eluted from the DynaBeads into a single low-bind 96-well polymerase chain reaction (PCR) plate (Eppendorf) for testing.")),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with maternal blood) (*see, e.g.*, Ex. 22 (https://www.progenity.com/products/innatal#practice) (listing under "Specimen Type" for the Innatal Prenatal Screen, "[w]hole blood specimens accepted; one 10 mL Streck tube"); Ex. 29 ("Venous blood (approximately 20 mL) was collected from study participants in a cell-free BCT tube (Streck. Omaha, NE, USA)."); Ex. 25 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/) (describing Streck cell-free DNA BCTs as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

67. Progenity has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the Innatal Prenatal Screen either itself, through its subsidiaries, and/or by directing and/or

controlling the performance of the claimed steps by third-party laboratories performing the Innatal Prenatal Screen. For example, Progenity uses the Innatal Prenatal Screen by collecting and analyzing samples sent to its laboratories for processing. (*See, e.g.*, Ex. 8 (https://www.progenity.com/products/innatal#basics) ("**Collect your sample**: Your healthcare provider will take a blood sample from your arm and send it to the Progenity laboratory.").)

68. In addition or in the alternative, Progenity has also induced infringement, and continue to induce infringement, of one or more claims of the '277 Patent under 35 U.S.C. § 271(b). Progenity actively, knowingly, and intentionally induces infringement of the '277 Patent by selling or otherwise supplying the Innatal Prenatal Screen with the knowledge and intent that third-party laboratories will use the Innatal Prenatal Screen supplied by Progenity to infringe the '277 Patent. Progenity acts with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Innatal Prenatal Screen and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the Innatal Prenatal Screen.

69. Progenity specifically intends and is aware that the ordinary and customary use of the Innatal Prenatal Screen would infringe the '277 Patent. For example, Progenity sells and provides the Innatal Prenatal Screen, which when used in its ordinary and customary manner intended and instructed by Progenity, infringes one or more claims of the '277 Patent, including at least claim 81. On information and belief, Progenity further provides product manuals and other instructional materials that cause its customers and partners to operate the Innatal Prenatal Screen for its ordinary and customary use. (*See, e.g.*, Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 18 ("We undertake efforts to increase the awareness and adoption of Innatal [] among laboratories, clinics, clinicians, physicians, payors, and patients."); *id.* at 33 ("A portion of our

tests are performed by third-party CLIA certified laboratories. These third-party laboratories are subject to contractual obligations[.]").) Progenity accordingly induces third parties to use Innatal Prenatal Screens in their ordinary and customary way to infringe the '277 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '277 Patent.

70. In addition or in the alternative, Progenity contributes to the infringement by third parties, such as health care providers or laboratories, of one or more claims of the '277 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, Innatal Prenatal Screens, knowing that those products constitute a material part of the inventions of the '277 Patent, knowing that those products are especially made or adapted to infringe the '277 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

71. As another example, Progenity infringes at least Claim 81 of the '277 Patent by making, selling and/or offering for sale in the United States, and/or importing into the United States, the Resura Prenatal Test. For example, use of the Resura Prenatal Test requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 21 (https://investors.progenity.com/news-releases/news-release-details/progenity-launches-first-commercially-available-custom-designed#:~:text=%C2%AB%20Back-,Progenity%20launches%20first%20commercially%20available%2C%20custom%2Ddesigned%2C%20noninvasive,prenatal%20test%20for%20monogenic%20diseases&text=Progenity%20also%20announces%20improvements%20to,across%2

0all%20common%20chromosomal%20aneuploidies) ("The Resura test uses fetal cell-free DNA (cfDNA) extracted from a sample of the mother's blood to test for genetic variants."); Ex. 31 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) ("Cell-free DNA is extracted from maternal plasma using an internally developed bead-based method")),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with maternal blood) (*see, e.g.*, Ex. 31 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) ("Blood is collected from pregnant patients at ≥ 10 weeks gestational age in a Streck BCT® and transported overnight to the Progenity lab."); Ex. 30 (https://www.progenity.com/products/resura#practice) ("**Step 3: Prenatal Testing**: A blood sample—six 10mL Streck DNA tubes—from the pregnant mother (10+ weeks' gestation) is required for prenatal testing."); Ex. 25 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/) (describing Streck cell-free DNA BCTs as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

72. Progenity has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the Resura Prenatal Test either itself, through its subsidiaries, and/or by directing and/or controlling the performance of the claimed steps by third-party laboratories performing the Resura Prenatal Test.

73. In addition or in the alternative, Progenity has induced infringement, and continues to induce infringement, of one or more claims of the '277 Patent under 35 U.S.C. § 271(b). Progenity actively, knowingly, and intentionally induces infringement of the '277 Patent by selling or otherwise supplying the Resura Prenatal Test with the knowledge and intent that third-party laboratories will use the Resura Prenatal Test supplied by Progenity to infringe the '277 Patent. Progenity acts with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Resura Prenatal Test and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the Resura Prenatal Test.

74. Progenity specifically intends and is aware that the ordinary and customary use of the Resura Prenatal Test would infringe the '277 Patent. For example, Progenity sells and provides the Resura Prenatal Test, which when used in its ordinary and customary manner intended and instructed by Progenity, infringes one or more claims of the '277 Patent, including at least claim 81. On information and belief, Progenity further provides product manuals and other instructional materials that cause its customers and partners to operate the Resura Prenatal Test for its ordinary and customary use. (*See, e.g.*, Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 33 ("A portion of our tests are performed by third-party CLIA certified laboratories. These third-party laboratories are subject to contractual obligations[.]"); Ex. 36 (https://www.progenity.com/draw-

locations) ("Your healthcare provider may direct you to one of Progenity's affiliated Patient Service Centers to collect your specimen for testing. . . . At your healthcare provider's office, you will receive a Specimen Collection Kit and a Test Requisition Form.").) Progenity accordingly induces third parties to use Resura Prenatal Tests in their ordinary and customary way to infringe the '277 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '277 Patent.

75. In addition or in the alternative, Progenity has contributed to the infringement by third parties, such as health care providers or laboratories, and continues to contribute to infringement by third parties, of one or more claims of the '277 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, Resura Prenatal Tests, knowing that those products constitute a material part of the inventions of the '277 Patent, knowing that those products are especially made or adapted to infringe the '277 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

76. Defendant Progenity has had knowledge of and notice of the '277 Patent and its infringement since at least the launch date of each of the infringing products.

77. Progenity's infringement of the '277 Patent has been, and continues to be, willful and deliberate since at least the launch date of each of the infringing products.

78. Ravgen has been and continues to be damaged by Progenity's infringement of the '277 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

79. Defendant's conduct in infringing the '277 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

COUNT II

Infringement Of The '720 Patent

80. Ravgen incorporates by reference paragraphs 1–79.

81. The '720 Patent is valid and enforceable.

82. Defendant Progenity has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including Progenity's Innatal Prenatal Screen and Resura Prenatal Test.

83. As one example, Progenity infringes at least claim 1 of the '720 patent by using the Innatal Prenatal Screen. For example, use of the Innatal Prenatal Screen requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as cell-free DNA) from a non-cellular fraction of a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 22 (https://www.progenity.com/products/innatal#practice) ("Cell-free DNA (cfDNA) is analyzed from a maternal blood sample to assess the pregnancy for common chromosome aneuploidies, including trisomy 21 (Down syndrome), trisomy 18, trisomy 13, and sex chromosome abnormalities."); *see also* Ex. 29 at 3 ("Sample tubes were shipped directly to Progenity, Inc. for processing and storage . . . . The plasma supernatants from 96 samples (including controls) were transferred to deep well plates (Arctic White; Bethlehem, PA, USA) for cfDNA isolation . . . . Isolated cfDNA samples were eluted from the DynaBeads into a single low-bind 96-well polymerase chain reaction (PCR) plate (Eppendorf) for testing.")),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; (such as cell-free DNA Streck tubes filled with maternal blood) (*see, e.g.*, Ex. 22 (listing under "Specimen Type" for the Innatal Prenatal Screen, "whole blood specimens accepted; one 10 mL Streck tube); Ex. 29 ("Venous blood (approximately 20 mL) was collected from study participants in a cell-free BCT tube (Streck. Omaha, NE, USA)."); Ex. 25 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/) (describing Streck cell-free DNA BCTs as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")),

c. detecting the presence or absence of the free nucleic acid (Ex. 22 (https://www.progenity.com/products/innatal#practice) ("The Innatal Prenatal Screen utilizes massively parallel sequencing (MPS) across the whole genome. This method sequences short fragments of DNA, creating millions of reads that are then mapped to the reference genome. The reads are counted to determine whether the sample has extra or missing reads from a particular chromosome. . . . Fetal fraction is determined for each sample[.]")).

84. Progenity has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the Innatal Prenatal Screen either itself, through its subsidiaries, and/or by directing and/or controlling the performance of the claimed steps by third-party laboratories performing the Innatal

Prenatal Screen. For example, Progenity uses the Innatal Prenatal Screen by collecting and analyzing samples sent to its laboratories for processing. (*See, e.g.*, Ex. 8 (https://www.progenity.com/products/innatal#basics) ("**Collect your sample**: Your healthcare provider will take a blood sample from your arm and send it to the Progenity laboratory.").)

85. In addition or in the alternative Progenity has also induced infringement, and continues to induce infringement, of one or more claims of the '720 Patent under 35 U.S.C. § 271(b). Progenity actively, knowingly, and intentionally induces infringement of the '720 Patent by selling or otherwise supplying the Innatal Prenatal Screen with the knowledge and intent that third-party laboratories will use the Innatal Prenatal Screen supplied by Progenity to infringe the '720 Patent. Progenity acts with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Innatal Prenatal Screen and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the Innatal Prenatal Screen.

86. Progenity specifically intends and is aware that the ordinary and customary use of the Innatal Prenatal Screen would infringe the '720 Patent. For example, Progenity sells and provides the Innatal Prenatal Screen, which when used in its ordinary and customary manner intended and instructed by Progenity, infringes one or more claims of the '720 Patent, including at least claim 1. On information and belief, Progenity further provides product manuals and other instructional materials that cause its customers and partners to operate the Innatal Prenatal Screen for its ordinary and customary use. (*See, e.g.*, Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 18 ("We undertake efforts to increase the awareness and adoption of Innatal and Preparent among laboratories, clinics, clinicians, physicians, payors, and patients."); *id.* at 33 ("A portion of our tests are performed by third-party CLIA certified laboratories. These third-party laboratories

are subject to contractual obligations[.]").) Progenity accordingly induces third parties to use Innatal Prenatal Screens in their ordinary and customary way to infringe the '720 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '720 Patent.

87. In addition or in the alternative, Progenity contributes to the infringement by third parties, such as health care providers or laboratories, of one or more claims of the '720 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, Innatal Prenatal Screens, knowing that those products constitute a material part of the inventions of the '720 Patent, knowing that those products are especially made or adapted to infringe the '720 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

88. As another example, Progenity infringes at least claim 1 of the '720 patent by using the Resura Prenatal Test. For example, use of the Resura Prenatal Test requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 21 (https://investors.progenity.com/news-releases/news-release-details/progenity-launches-first-commercially-available-custom-designed#:~:text=%C2%AB%20Back-,Progenity%20launches%20first%20commercially%20available%2C%20custom%2Ddesigned%2C%20noninvasive,prenatal%20test%20for%20monogenic%20diseases&text=Progenity%20also%20announces%20improvements%20to,across%20all%20common%20chromosomal%20aneuploidies) ("The Resura test uses fetal cell-free DNA (cfDNA) extracted from a sample of the mother's blood to test for

genetic variants."); Ex. 31 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) ("Cell-free DNA is extracted from maternal plasma using an internally developed bead-based method")),

a. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with maternal blood) (*see, e.g.*, Ex.32 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) ("Blood is collected from pregnant patients at ≥ 10 weeks gestational age in a Streck BCT® and transported overnight to the Progenity lab."); Ex. 30 (https://www.progenity.com/products/resura#practice) ("**Step 3: Prenatal Testing**: A blood sample—six 10mL Streck DNA tubes—from the pregnant mother (10+ weeks' gestation) is required for prenatal testing."); Ex. 25 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/) (describing Streck cell-free DNA BCTs as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

b. detecting the presence or absence of the free nucleic acid (Ex. 30 (https://www.progenity.com/products/resura#practice) ("The test looks for common chromosomal diseases along with the specific monogenic disease for

which testing is requested."); Ex. 31 (https://www.progenity.com/sites/default/files/2018_NSGC%20Poster_Prenatal%20testing%20for%20monogenic%20disease_FINAL.pdf) ("**Data analysis:** The total fetal DNA contribution, the cfDNA allele ratio, and other run-based data are used to calculate the fetal status (affected vs. unaffected) and the associated probability.")).

89. Progenity has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the Resura Prenatal Test either itself, through its subsidiaries, and/or by directing and/or controlling the performance of the claimed steps by third-party laboratories performing the Resura Prenatal Test.

90. In addition or in the alternative, Progenity has induced infringement, and continues to induce infringement, of one or more claims of the '720 Patent under 35 U.S.C. § 271(b). Progenity actively, knowingly, and intentionally induces infringement of the '720 Patent by selling or otherwise supplying the Resura Prenatal Test with the knowledge and intent that third-party laboratories will use the Resura Prenatal Test supplied by Progenity to infringe the '720 Patent. Progenity acts with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Resura Prenatal Test and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the Resura Prenatal Test.

91. Progenity specifically intends and is aware that the ordinary and customary use of the Resura Prenatal Test would infringe the '720 Patent. For example, Progenity sells and provides the Resura Prenatal Test, which when used in its ordinary and customary manner intended and

instructed by Progenity, infringes one or more claims of the '720 Patent, including at least claim 1. On information and belief, Progenity further provides product manuals and other instructional materials that cause its customers and partners to operate the Resura Prenatal Test for its ordinary and customary use. (*See, e.g.*, Ex. 20 (Excerpt of Progenity, Inc. Prospectus, June 2020) at 33 ("A portion of our tests are performed by third-party CLIA certified laboratories. These third-party laboratories are subject to contractual obligations[.]"); Ex. 36 (https://www.progenity.com/draw-locations) ("Your healthcare provider may direct you to one of Progenity's affiliated Patient Service Centers to collect your specimen for testing. . . . At your healthcare provider's office, you will receive a Specimen Collection Kit and a Test Requisition Form.").) Progenity accordingly induces third parties to use Resura Prenatal Tests in their ordinary and customary way to infringe the '720 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '720 Patent.

92. In addition or in the alternative, Progenity has contributed to the infringement by third parties, such as health care providers or laboratories, and continues to contribute to infringement by third parties, of one or more claims of the '720 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, Resura Prenatal Tests, knowing that those products constitute a material part of the inventions of the '720 Patent, knowing that those products are especially made or adapted to infringe the '720 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

93. Defendant Progenity has had knowledge of and notice of the '720 Patent and its infringement since at least the launch date of each of the infringing products.

94. Progenity's infringement of the '720 Patent has been, and continues to be, willful and deliberate since at least the launch date of each of the infringing products.

95. Ravgen has been and continues to be damaged by Progenity's infringement of the '720 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

96. Progenity's conduct in infringing the '720 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Ravgen prays for judgment as follows:

A. That Progenity, Inc. has infringed each of the Patents-in-Suit;

B. That Progenity's infringement of each of the Patents-in-Suit has been willful;

C. That Ravgen be awarded all damages adequate to compensate it for Progenity's past infringement and any continuing or future infringement of the Patents-in-Suit up until the date such judgment is entered, including pre- and post-judgment interest, costs, and disbursements as justified under 35 U.S.C. § 284;

D. That any award of damages be enhanced under 35 U.S.C. § 284 as result of Progenity's willful infringement;

E. That this case by declared an exceptional case within the meaning of 35 U.S.C. § 285 and that Ravgen be awarded the attorney fees, costs, and expenses incurred in connection with this action;

F. That Ravgen be awarded either a permanent injunction, or, at least, a compulsory ongoing licensing fee; and

F. That Ravgen be awarded such other and further relief at law or equity as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiff Ravgen hereby demands a trial by jury on all issues so triable.

Dated: December 21, 2020

Respectfully submitted,

FARNAN LLP

/s/ Michael J. Farnan
Brian E. Farnan (Bar No. 4089)
Michael J. Farnan (Bar No. 5165)
919 N. Market St., 12th Floor
Wilmington, DE 19801
Telephone: (302) 777-0300
Facsimile: (302) 777-0301
bfarnan@farnanlaw.com
mfarnan@farnanlaw.com

Attorneys for Plaintiff Ravgen, Inc.

Of Counsel:

John M. Desmarais
Kerri-Ann Limbeek
Jamie L. Kringstein
Brian D. Matty
Michael Ling
Deborah J. Mariottini
Email: jdesmarais@desmaraisllp.com
Email: klimbeek@desmaraisllp.com
Email: jkringstein@desmaraisllp.com
Email: bmatty@desmaraisllp.com
Email: mling@desmaraisllp.com
Email: dmariottini@desmaraisllp.com
DESMARAIS LLP
230 Park Avenue
New York, NY 10169
Telephone: 212-351-3400
Facsimile: 212-351-3401